Prasugrelはクロピドグレルよりもイベントを減少させなかった

TRILOGY ACS:血行再建術を施行しない急性冠症候群の薬物療法においてprasugrelとクロピドグレルとで差はなかった

TRILOGY ACS: No difference between prasugrel and clopidogrel for medical treatment of acute coronary syndromes without revascularization

血行再建術を施行せず薬物療法で管理した急性冠症候群患者の血小板阻害効果を調査した初めてのトライアルの結果、死亡、心筋梗塞または脳卒中予防効果においてprasugrelとクロピドグレルとでは有意差がないことが示された。この第III相試験である、Targeted Platelet Inhibition to Clarify the Optimal Strategy to Medically Manage Acute Coronary Syndromes（TRILOGY ACS）スタディでは、血行再建術を施行せずに管理した不安定狭心症または非ST上昇心筋梗塞のACS患者（7,243人、75歳未満）においてprasugrel（1日10mg）をクロピドグレル（1日75mg）と最長30か月間比較した。経過観察（中央値17か月）における一次エンドポイント（心血管死、心筋梗塞、または脳卒中）が発現したのはprasugrel群で13.9%でありクロピドグレル群で16.0%であった（HR 0.91; 95% CI 0.79-1.05; *P* =0.21）。予想外なことに、prasugrel群では12か月後の虚血性イベントの低リスク傾向を有し、時間依存性な治療効果が認められた。さらに、全ての多発性再発性虚血イベントを評価する予め特定された解析において、prasugrelによりリスクが低下することが示唆された（HR 0.85; 95% CI 0.72-1.00; *P* =0.044）。重篤な出血性合併症は頻度が低くそれぞれの治療群で同程度であった。この結果は2012年European Society of Cardiology学会で発表され、*New England Journal of Medicine*オンライン版で発表された。

Full Text

The first trial to study the effect of platelet inhibition in patients with acute coronary syndromes managed medically without revascularization has found no significant difference between prasugrel and clopidogrel in the prevention of death, myocardial infarction or stroke.

The findings, from the phase III Targeted Platelet Inhibition to Clarify the Optimal Strategy to Medically Manage Acute Coronary Syndromes (TRILOGY ACS) study, were presented at a Hot Line session of ESC Congress 2012 in Munich and simultaneously published online in the New England Journal of Medicine.

TRILOGY ACS was double-blind, randomized trial in which the effect of prasugrel (10 mg daily) was compared with that of clopidogrel (75 mg daily) for up to 30 months of treatment in ACS patients under 75 years with unstable angina or non-ST elevation myocardial infarction (non-STEMI) managed without revascularization. All study subjects, who totaled 7243 in number, were taking aspirin, and the prasugrel dose was reduced to 5 mg daily for patients weighing less than 60 kilograms. The primary end point of the trial was cardiovascular death, myocardial infarction, or stroke. The study was performed at 966 sites in 52 countries.

Results showed that, through a median follow-up period of 17 months, the primary end point among participants under 75 years occurred in 13.9% of those treated with prasugrel and 16.0% of those treated with clopidogrel (HR 0.91; 95% CI 0.79-1.05; P=0.21). Similar results were observed in the overall patient population of 9326 patients, who included an additional 2083 patients aged 75 years or older in whom a reduced dose of prasugrel (5 mg daily) vs. clopidogrel (75 mg daily) was explored.

However, an unexpected, time-dependent treatment effect was observed with a trend for a lower risk of ischemic events with prasugrel after 12 months among patients under 75 years of age. Furthermore, a pre-specified analysis, which accounted for all multiple recurrent ischemic events (not just the first event among all components of the primary end point) suggested a lower risk with prasugrel (HR 0.85; 95% CI 0.72-1.00; P=0.044).

The rates of major, life-threatening, fatal and intracranial bleeding were infrequent and similar in each treatment group, both in patients over 75 years and in the overall population. The frequency of non-hemorrhagic serious adverse events was also similar by treatment, except for a higher frequency of heart failure in the clopidogrel group.

As background to the study, the study's chairman, Professor E Magnus Ohman from Duke University Medical Center, Durham, USA, explained that the patient population of the TRILOGY ACS trial has not been exclusively studied before in a randomized trial. Around 60% of ACS patients undergo revascularization, but the remaining 40% are managed solely with drug therapy. "Patients who are medically managed are at higher risk for repeated cardiovascular-related events," said Professor Ohman. "So optimizing medical therapy for these patients is extremely important."

The efficacy and safety of prasugrel and clopidogrel were first compared in the TRITON study of 2007 in ACS patients scheduled for PCI. This study found that prasugrel was associated with significantly lower rates of ischemic events, including stent thrombosis, but with an increased risk of major bleeding. TRILOGY ACS, said Professor Ohman, was designed as a follow-up to the TRITON trial, "to see if prasugrel was just as effective in ACS patients who aren't getting coronary stents or coronary bypass surgery".

The TRILOGY ACS study did not find an increase in severe bleeding complications with prasugrel as seen in the TRITON study, albeit with modification of the prasugrel dose for low-body weight (weight <60 kilograms) and elderly patients.

"This trial is unique in that it studied a population we have not previously explored in such detail," said Professor Ohman. "The result being neutral raises many important questions. The fact that prasugrel appears safe - with no statistical increase in major bleeding - offers assurance of the prolonged safety of this therapy, which had been raised in previous trials."

Adding further comment on the results, Dr. Matthew T. Roe, Associate Professor of Medicine, Division of Cardiology, Duke University Medical Center, said: "We studied the use of potent platelet inhibition for a longer duration of treatment than any previous trial in a previously under-studied population of ACS patients. While we did not achieve our primary objective, we showed no difference in serious bleeding complications between prasugrel and clopidogrel, and we observed several intriguing findings that we feel deserve further exploration."

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Conference News